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## Short Communication

## Six-year experience of detection and investigation of possible Middle East Respiratory Syndrome coronavirus cases, England, 2012–2018



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## ABSTRACT

**Objectives:** Surveillance for Middle East Respiratory Syndrome (MERS) has been undertaken in the UK since September 2012. This study describes the surveillance outcomes in England from 2012 to 2018.

**Study design:** This was a descriptive study using surveillance data.

**Methods:** Local health protection teams in England report possible MERS cases to the National Infection Service with clinical and laboratory data.

**Results:** A total of 1301 possible MERS cases were identified in the study period. Five cases were laboratory-confirmed MERS. The majority of cases had travelled to Saudi Arabia (56.7%) and United Arab Emirates (25.9%). Fifty-four percent of cases were men and 43.7% were women. The majority of cases (65.1%) were aged 45 years or older. The number of tests increased in the period after Hajj each year. Laboratory-confirmed alternative diagnoses were available for 513 (39.4%) cases; influenza was the most common virus detected ( $n = 255$ , 52.4%).

**Conclusions:** Our study highlights the importance of differential diagnosis of influenza and other respiratory pathogens and early influenza antiviral treatment.

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Coronaviruses are a large family of viruses that infect animals and humans.<sup>1</sup> Seasonal human coronavirus infections are typically associated with cold or influenza-like illnesses. However, coronaviruses have the potential to cause severe transmissible human disease, as demonstrated by the severe acute respiratory syndrome outbreak between 2002 and 2003<sup>2</sup> and the currently ongoing coronavirus disease 2019 pandemic in 2020.<sup>3</sup>

The Middle East Respiratory Syndrome coronavirus (MERS-CoV) is a betacoronavirus that was first identified in 2012.<sup>4</sup> The first case of Middle East Respiratory Syndrome (MERS) to be recognised occurred in the Kingdom of Saudi Arabia (KSA) and was reported in September 2012.<sup>5</sup> In the same month, the UK reported the second infection to be identified globally, in a Qatari national with a travel history to KSA.<sup>4</sup>

MERS is not a notifiable disease in the UK, but an enhanced surveillance programme for MERS has been in place in England

since 2012, consisting of rapid identification and investigation of possible cases presenting to the UK health system, awareness-raising activities and implementation of rapid, enhanced respiratory infection prevention and control measures for suspected and confirmed cases. This surveillance is important not only for early detection and treatment of cases but also to prevent onward spread of the disease, particularly outbreaks in hospital settings, which have been seen elsewhere, especially in the Middle East and the Republic of South Korea.<sup>6</sup> This study describes the results of this national MERS surveillance system in England from September 2012 to September 2018.

After the first imported MERS case in the UK was confirmed,<sup>4</sup> in September 2012, this MERS surveillance system was set up. Clinicians in England are requested to report possible cases that meet the criteria set out in the national investigation algorithm<sup>7</sup> to local Public Health England (PHE) health protection teams (HPTs). The details of the possible case definition and procedures of investigation are listed in the national investigation algorithm.<sup>7</sup> HPTs record possible cases via the national case and outbreak management

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system (HPZone) and send a minimum data set form to the PHE national surveillance team, based at the National Infection Service. The minimum data set form collects key data including demographics, clinical details, travel and contact history and results of laboratory testing. The possible case criteria have evolved over time, particularly in 2018 when they were adapted to include milder presentations.<sup>7</sup> All diagnostic testing performed by PHE public health laboratories is reported via the national laboratory surveillance system, the respiratory DataMart database,<sup>8</sup> and confirmatory testing is performed solely by the PHE national reference laboratory. Diagnostic testing for MERS-CoV RNA was included in a routine panel of respiratory viruses tested for by qualitative real-time reverse transcription polymerase chain reaction, as described elsewhere. The routine panel included testing for influenza A (both H1 and H3), influenza B, respiratory syncytial virus (RSV), rhinoviruses, parainfluenza virus type 1–4, human metapneumovirus (hMPV) and adenoviruses. Descriptive analyses were carried out to summarise the epidemiological and laboratory test results.

In total, 1301 patients in England were investigated and underwent testing for possible MERS-CoV infection between 22 September 2012 and 30 September 2018. Of these, five tested positive for MERS-CoV infection, including confirmatory testing by the PHE national reference laboratory (3 imported cases and two associated secondary transmission cases). The remaining 1296 possible cases tested negative. The first confirmed MERS case in the UK was reported to the World Health Organization (WHO) on 22 September 2012, and details of this case have been published.<sup>4</sup> The most recent confirmed imported UK case was reported to the WHO on 22 August 2018.<sup>9</sup> Despite extensive contact tracing around these imported cases, no healthcare workers caring for these cases have been found to have been infected in England.

Of all the 1301 investigated patients that underwent laboratory testing for MERS-CoV, 54.0% of them were men and 43.7% were women (2.3% gender unknown); 39.6% of the cases were aged 45–64 years, 29.3% were 15–44 years and 26.1% were older than 65 years. The greatest number of tests was performed in London (281, 33.3%) based on patients' residential addresses and available data from 64.9% (844/1301) patients. The frequency of testing increased in the period after the Hajj each year, usually between August and October. The majority of cases investigated had a travel history to KSA (56.7%, 362/638) and United Arab Emirates (UAE, 25.9%, 165/638), whereas other cases had a travel history to Kuwait (4.4%, 28/638), Qatar (4.1%, 26/638), Oman (2.4%, 15/638) and other countries including Jordan (n = 13), Bahrain (n = 11), Iraq (n = 9), Iran (n = 6) and Yemen (n = 3).

The clinical and epidemiological characteristics among all investigated patients (where information is available) are summarised in Table 1. Fever (95.7%) and cough (93.9%) were the most commonly reported symptoms. Pulmonary parenchymal involvement was reported in the majority of investigated patients (79.5%). Acute respiratory distress syndrome and the requirement for mechanical ventilation were reported in 12.9% and 9.4% of cases, respectively, while extracorporeal membrane oxygenation (ECMO) was administered in only 1.4% of investigated cases. Most cases (96.8%) were reported to have been hospitalised.

As only a small number (n = 5) of all possible cases (n = 1301) during the six-year study period were laboratory-confirmed MERS (Table 2), the proportion of possible cases that were confirmed according to a range of clinical criteria was mostly low. However, the likelihood of MERS confirmation increased with disease severity, with three of the seven possible cases who received ECMO being confirmed as MERS-CoV infected.

Laboratory-confirmed alternative diagnoses were available for 513 (39.4%, 513/1301) of all possible cases. Influenza virus (alone or

**Table 1**

Clinical and epidemiological characteristics among all investigated patients where information available in the MERS-CoV surveillance system, England, 2012–2018 (n = 1301).

| Characteristics  | No. (%) patients | No. (%) MERS-CoV positive |
|--|------------------|---------------------------|
| Age group (years)  |                  |                           |
| 0–4  | 38 (2.9)         | 0 (0.0)                   |
| 5–14   | 23 (1.8)         | 0 (0.0)                   |
| 15–44  | 381 (29.3)       | 2 (0.5)                   |
| 45–64  | 515 (39.6)       | 2 (0.4)                   |
| 65+  | 339 (26.1)       | 1 (0.3)                   |
| Unknown  | 5 (0.4)          | 0 (0.0)                   |
| Sex  |                  |                           |
| Male   | 703 (54.0)       | 4 (0.6)                   |
| Female   | 568 (43.7)       | 1 (0.2)                   |
| Unknown  | 30 (2.3)         | 0 (0.0)                   |
| Clinical history   |                  |                           |
| Fever  | 288/301 (95.7)   | 3 (1.0)                   |
| Cough  | 277/295 (93.9)   | 3 (1.1)                   |
| Pulmonary parenchymal involvement  | 306/385 (79.5)   | 3 (1.0)                   |
| Acute respiratory distress syndrome  | 55/428 (12.9)    | 3 (5.5)                   |
| Mechanical ventilation   | 49/520 (9.4)     | 3 (6.1)                   |
| Extracorporeal membrane oxygenation (ECMO)   | 7/483 (1.4)      | 3 (42.9)                  |
| Hospitalisation  | 607/627 (96.8)   | 4 (0.7)                   |
| Travel history to Middle East countries in exposure period <sup>a</sup> before symptom onset | 638/641 (99.5)   | 3 (0.5)                   |

MERS-CoV, Middle East Respiratory Syndrome coronavirus.

<sup>a</sup> Exposure period was 10 days until June 2013 when it was increased to 14 days.

as a coinfection with other pathogens) was the most common pathogen (n = 269, 52.4%), followed by rhinovirus (alone or as a coinfection with other pathogens, n = 158, 30.8%), adenovirus (alone or as a coinfection with other pathogens, n = 38, 7.4%), parainfluenza virus (alone or as a coinfection with other pathogens, n = 27, 5.3%), hMPV (alone or as a coinfection with other pathogens, n = 23, 4.5%), RSV (alone or as a coinfection with other pathogens n = 18, 3.5%) and Legionella species (n = 15, 2.9%). Coinfections with two or more pathogens were found in 47 of 513 (9.2%) possible cases. Among the five confirmed MERS cases, four had a coinfection with either influenza (one case), or parainfluenza (two cases), or adenovirus (one case). Among the 15 Legionella cases, ten were returning travellers from the UAE, four from other Middle East countries and one had unknown travel history. This is likely to reflect the previously reported observations of Legionnaires' disease associated with travel to Dubai, UAE.<sup>10</sup>

## Discussion

We provide an overview of six-year enhanced MERS surveillance in England. The vast majority (94.9%) of possible MERS cases were those aged 15 years and older. More possible cases were tested in London than in any other area in England, which may be due to the larger population in London, its ethnically diverse population and associated travel patterns to the Middle East, including Hajj pilgrimages. Differences in awareness regarding MERS between rural locations and cities might also play a role in possible case reporting practice. We reported four confirmed cases in 2012 and 2013; and only limited, non-sustained secondary transmission was associated with the second confirmed case. An additional confirmed imported case was detected in August 2018.<sup>9</sup> We found that the likelihood of MERS confirmation increased with increasing disease severity. We also found that MERS-CoV testing in England peaked annually after the Hajj pilgrimage; therefore, laboratories, hospitals and HPTs should be prepared for these peak activity periods, both in terms of requirements for testing and the additional

**Table 2**

Clinical details of the five laboratory-confirmed MERS-CoV cases, England, 2012–2018.

|                                     | Case 1      | Case 2                  | Case 3 (contact of Case 2) | Case 4 (contact of Case 2) | Case 5       |
|-------------------------------------|-------------|-------------------------|----------------------------|----------------------------|--------------|
| Age group (years)                   | 45–64       | 45–64                   | 15–44                      | 15–44                      | 65+          |
| Sex                                 | Male        | Male                    | Male                       | Female                     | Male         |
| Onset month and year                | August 2012 | January 2013            | February 2013              | February 2013              | August 2018  |
| Country of residence                | Qatar       | England                 | England                    | England                    | Saudi Arabia |
| Fever                               | Yes         | Yes                     | Unknown                    | Unknown                    | Yes          |
| Cough                               | Yes         | Yes                     | Unknown                    | Unknown                    | Yes          |
| Pulmonary parenchymal involvement   | Yes         | Yes                     | Yes                        | No                         | No           |
| Acute respiratory distress syndrome | Yes         | Yes                     | Yes                        | No                         | No           |
| Mechanical ventilation              | Yes         | Yes                     | Yes                        | No                         | No           |
| ECMO                                | Yes         | Yes                     | Yes                        | No                         | No           |
| Hospitalisation                     | Yes         | Yes                     | Yes                        | No                         | Yes          |
| Coinfection                         | No          | Influenza A (H1N1)pdm09 | Parainfluenza-2            | No                         | Adenovirus   |
| Travel history                      | Yes         | Yes                     | No                         | No                         | Yes          |
| Outcome                             | Died        | Died                    | Died                       | Recovered                  | Recovered    |

MERS-CoV, Middle East Respiratory Syndrome coronavirus; ECMO, extracorporeal membrane oxygenation.

resources required for the appropriate infection prevention and control measures. In addition, 39% of all possible cases had alternative diagnoses identified, mainly influenza, but also other important pathogens such as *Legionella* species. We must emphasise that influenza and *Legionella* infections are not only important but also treatable diseases.

The main limitation of this study is likely to be the incomplete reporting. Minimum data set forms were only received for 57.0% (742/1301) of all laboratory-tested cases. MERS is not notifiable in the UK, and some possible cases are not reported to HPTs. In part, this may be because not all persons tested met the ‘possible case’ definition as advised by PHE.<sup>7</sup> In addition, since July 2017, MERS-CoV testing is no longer provided solely by PHE and other clinical diagnostic laboratories were able to implement their own testing; therefore, some possible cases may not have been reported to the national surveillance systems. Another limitation is that our database only contains records of positive laboratory test results for other respiratory pathogens, such as influenza and rhinovirus detections, but we do not have records of negative test results. Therefore, the proportion positive for non-MERS-CoV pathogen infections could not be calculated in our data.

Coinfections are not uncommon in MERS cases; therefore, a positive detection of influenza or other pathogens does not exclude MERS. This study shows the importance of a national surveillance system not only for MERS but also for any other emerging severe infections to ensure prompt investigation and implementation of appropriate infection control measures and appropriate laboratory testing. Transmission of MERS-CoV continues in the Middle East, and on-going vigilance is required.

## Author statements

### Ethical approval

Not required (this is part of the national surveillance work carried out by a government agency to monitor and control infection disease for public health purpose).

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None.

### Competing interests

There are no competing interests.

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